

Urinary levels of intact, free beta and beta core fragment of human chorionic gonadotrophin (hCG) in early pregnancy

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Introduction

- Home and laboratory pregnancy testing relies on the detection of human chorionic gonadotrophin (hCG),¹ a glycoprotein with two non-covalently linked subunits: alpha (hCG- α) and beta (hCG- β)
- Multiple forms of hCG are present in the serum and urine of pregnant women: as shown in Figure 1
- The degradation product, β -core-hCG is only present in urine and becomes the predominate form detectable in later pregnancy.

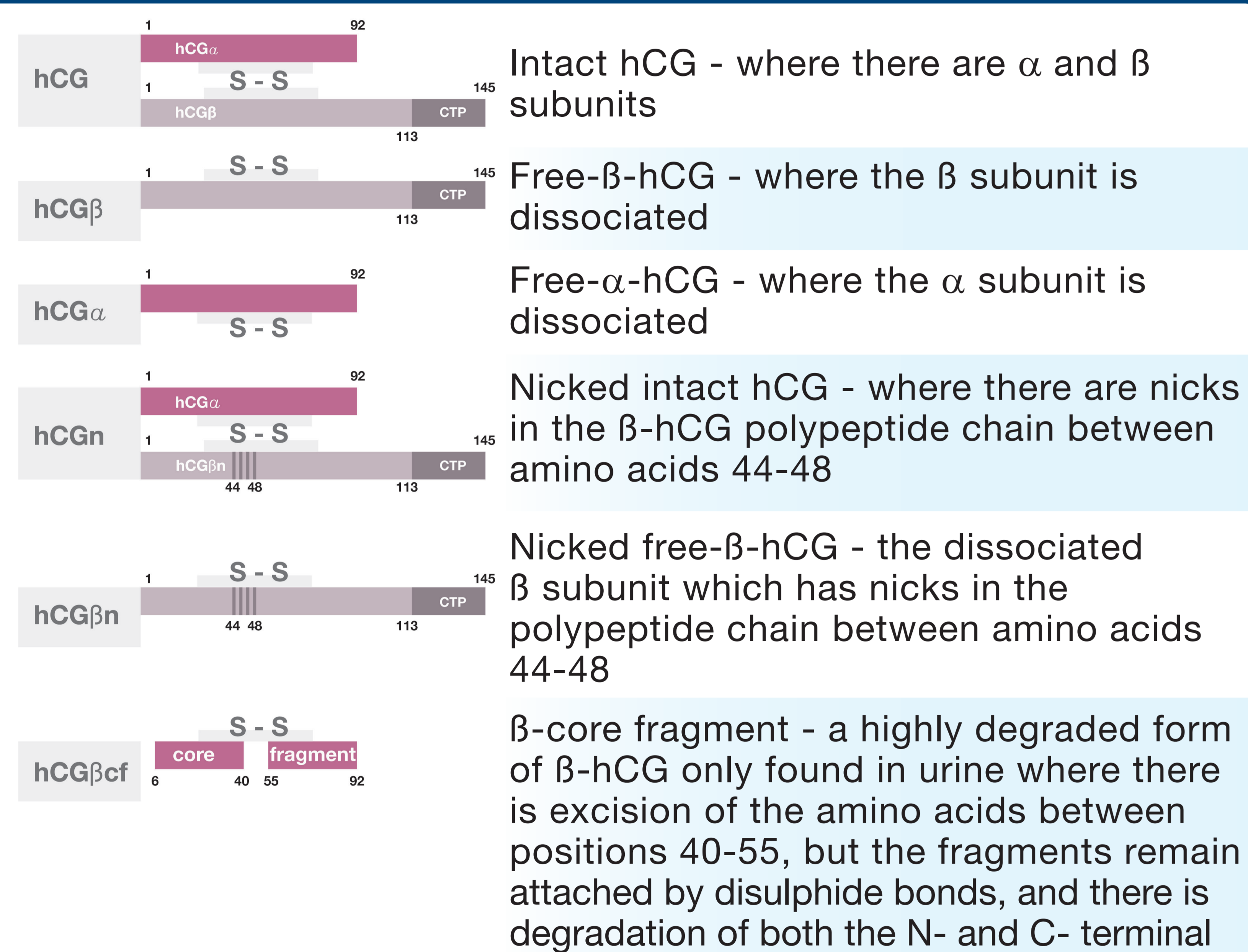


Figure 1: Structure of the different forms of hCG²

- Reference ranges have been published for intact urinary hCG, but not for other forms present in the urine of pregnant women^{1,3}
- Free- β -hCG and β -core-hCG have a different profile of daily rise compared with intact hCG
- Very high levels of β -core-hCG, that can occur in later pregnancy, have caused false negative point-of-care pregnancy test results which can have serious clinical consequences
- Although laboratory testing for β -core-hCG interference has been conducted on both home and point-of-care pregnancy tests, there is some debate as to what the most appropriate testing methodology should be^{4,5}
- The ratio of intact: free- β -hCG has been related to pregnancy viability⁶
- Therefore, it is important to obtain further understanding of the ranges of these forms of hCG in pregnancy and their relationship with the total level of hCG.

Purpose of the study

- This study sought to improve the understanding of the levels of free- β and β -core-hCG in viable pregnancies.

Methods

- Daily early morning urine samples were collected from women with viable pregnancies throughout early pregnancy
- The samples were collected pre-conception to enable the day of ovulation to be determined for each woman by the detection of the LH surge (AutoDELFI quantitative LH assay, with ovulation presumed as LH surge + 1 day). This enabled accurate assignment of pregnancy duration for each volunteer
- Intact, free- β and β -core-hCG were measured using AutoDELFI immunoassays, using in-house reagents for β -core-hCG assays, and the Perkin Elmer assay for intact hCG and free- β assays.
- Mean and standard deviations (SD) by the day of pregnancy were derived.

Results

- Figure 2 shows the levels of intact hCG, free β -hCG and β -core-hCG in the first trimester of pregnancy

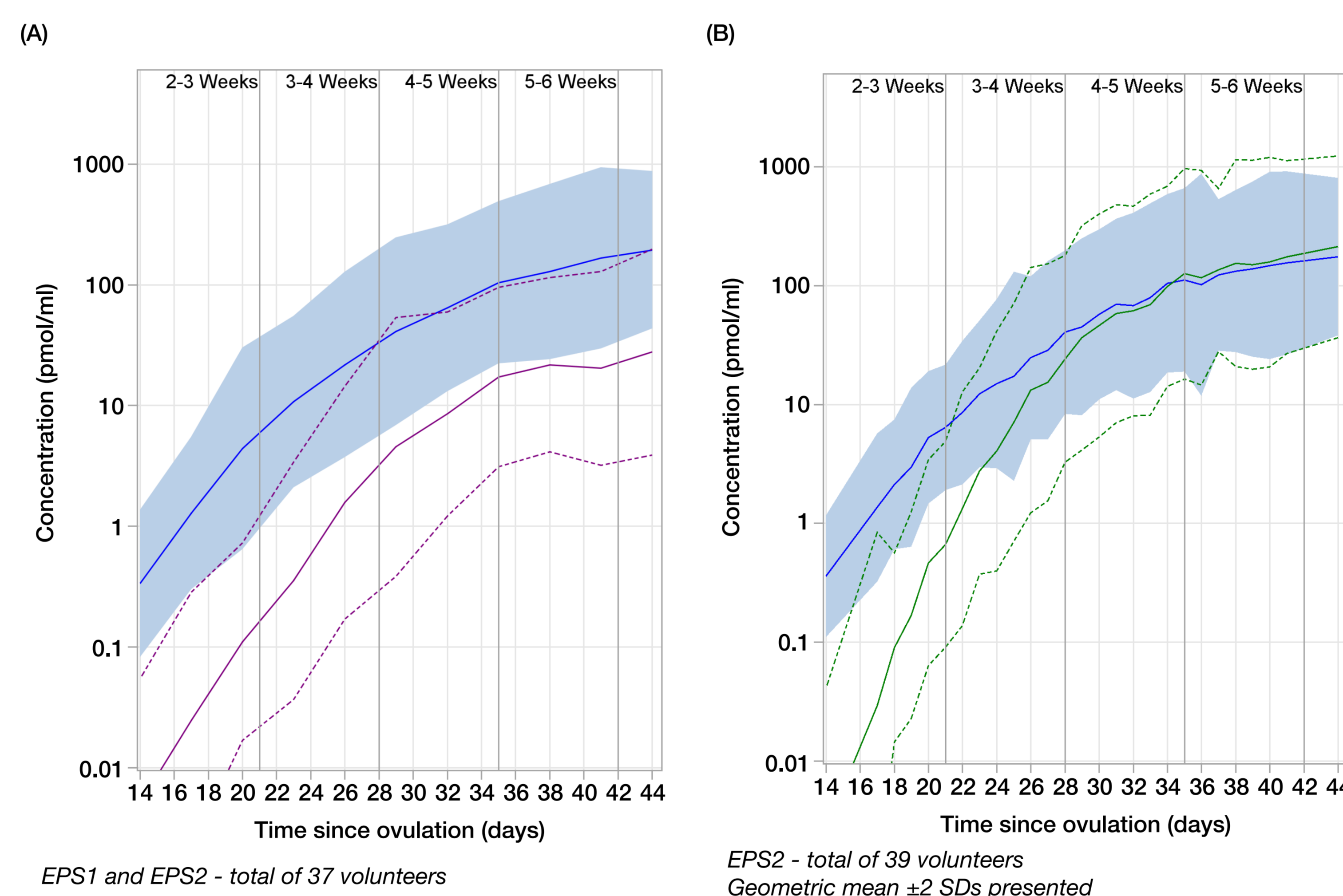


Figure 2: Intact hCG, free β -hCG (A) and β -core-hCG (B) concentrations during the first trimester of pregnancy

- As expected, intact hCG was present in the urine of pregnant women 8 days following ovulation, and showed a consistent rise throughout early pregnancy
- However, free β -hCG was not consistently detectable in urine until day 21
- Free β -hCG appeared in urine at a constant ratio of approximately 1:100 of intact hCG
- β -core-hCG had a different profile, appearing in urine later than intact hCG (day 19), yet becoming the predominant form by day 35
- High levels of β -core-hCG were only present when there was also intact hCG in the sample
- The minimum level of intact hCG in samples with β -core-hCG >500,000 pmol/l was 10,003 pmol/l (4017 mIU/ml), as shown in Figure 3.

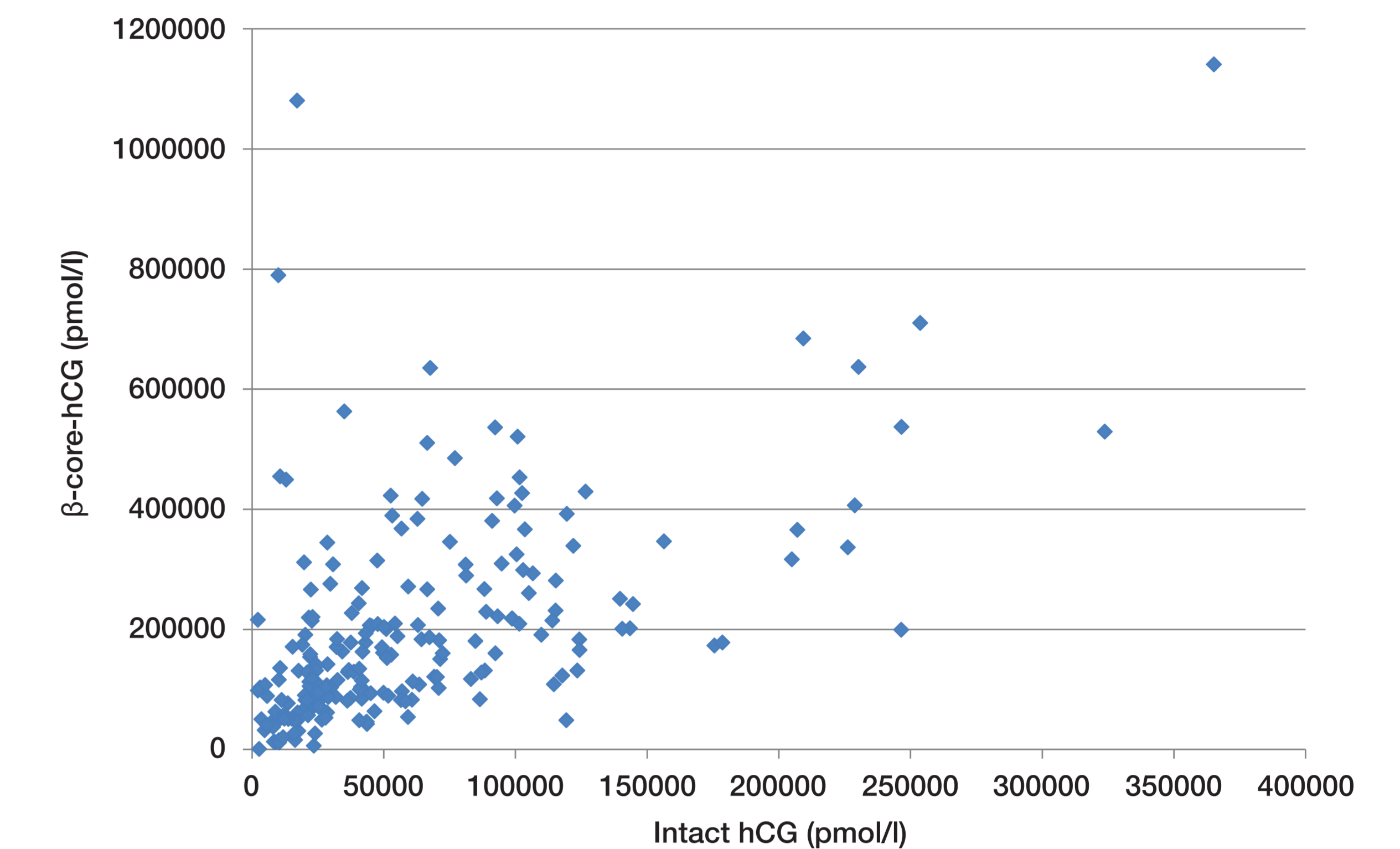


Figure 3: Paired intact hCG: β -core-hCG measurements in urine samples from women who were 6–12 weeks pregnant

Conclusions

- The urinary ranges of free- β and β -core-hCG in viable pregnancies provide a valuable reference tool
- While free- β hCG appears to be a constant proportion of intact hCG throughout early pregnancy, β -core-hCG does not have the same direct relationship
- Although urine levels of β -core-hCG in early pregnancy are negligible, concentrations can reach 500,000 pmol/l by day 28 post ovulation in pregnant women; this level has been shown to cause false negatives in some pregnancy tests
- As these high levels of β -core-hCG always occur in the presence of total hCG, testing for interference of assays by β -core-hCG should be conducted using samples that also contain intact hCG
- Only assays that demonstrate they are unaffected by β -core-hCG interference should be used in later pregnancy.

References

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Declaration of Interest

This study was funded by SPD Development Company Ltd., a wholly owned subsidiary of SPD Swiss Precision Diagnostics GmbH. Sarah Johnson, Saji Eapen and Lorrae Marriot are employees of SPD Development Company Ltd.

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